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The Keystone Center
Keystone, Colorado

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THE KEYSTONE CENTER'S
1992 SCIENTIST TO SCIENTIST COLLOQUIUM
MEETING SUMMARY

August 15 - 20, 1992
Keystone, Colorado

The Keystone Center, founded in 1975, is a national non-profit organization located in the Rocky Mountains at Keystone, Colorado, 75 miles west of Denver. The Center is organized around three major programmatic areas: (1) The Keystone Science and Public Policy Program, which facilitates the resolution of national public policy conflicts through the use of an innovative consensus dialogue approach; (2) The Keystone Science School Program, which provides residential natural science education programs for students of all ages with emphasis on sound scientific understanding of nature and our relationship to the environment; (3) The Symposia on Molecular and Cellular Biology, which offers an annual series of colloquies addressing critical developments in science and research. The Center's programs are funded by grants from foundations, corporations, government, individuals, and in the case of the Science School Program, fees paid by students.

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PREFACE

For the second consecutive summer, The Keystone Center brought together leading American scientists, from all disciplines, for the Scientist to Scientist Colloquium. Created by The Keystone Center and a planning committee of distinguished scientists from the major fields, the first Colloquium was held in 1991. The goal was, and still is, to bring together leading researchers and other members of the scientific community to share with each other what kind of work they do at the outer reaches of science, why it is so compelling to them, and why others should also be excited as they gain some understanding beyond their own fields. The Keystone Center feels that this kind of interdisciplinary communication is lacking in the scientific community and must be encouraged.

The 1992 Scientist to Scientist Colloquium was held August 15-20 in Keystone, Colorado. The chairman of this year's Steering Committee was **Dr. Eric Lander**, Member of the Whitehead Institute for Biomedical Research, and the co-chair was **Dr. Ronald Cape**, co-founder of Darwin Technologies, Inc. Seven major topics were addressed over a five-day period, including: Evolution, High Precision Physics, Chemistry, Managing Science: What Works?, Astrophysics, Immunology, and Computer Science. In addition to these formal presentations, small, diverse groups were organized by general participants to address other important issues facing the scientific community. "Science Education: What is the Role of the Professional Scientist?," "Women in Science," and "How Should American Scientists and Science Funding Agencies Relate to Japanese Science and Technology Initiative?" are the titles of a few of these discussions.

Each major session consisted of a topic chair, who introduced the subject matter, and two speakers who presently investigate cutting-edge issues or developments in their respective fields. The summary that follows includes a brief synopsis of each speaker's presentation and an attempt to give a flavor of the discussion that followed. The discussions, although not emphasized in the individual summaries, were perhaps the most fruitful facet of the Colloquium. Equal time was given to the participants to ask questions not only about the subject matter of the presentations, but also about attitudes, assumptions, approaches, and concerns that are particular to a field of study. Questions such as, "What is the definition of a cell?" and "Where are we located in the universe?" seemed simple and straightforward, but the discussions that evolved from such questions illuminated the differences that exist between scientific disciplines. The observations of one conferee contained in the enclosed editorial of Bio/Technology may give a more intimate sense of the proceedings of the 1992 Colloquium.

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The Keystone Center is grateful for the support given by all funders who made the 1992 Scientist to Scientist Colloquium possible:

The Alfred P. Sloan Foundation
The Department of the Navy, Office of Naval Research
Nature Publishing Company and Bio/Technology Magazine
AT&T Bell Laboratories

Already The Keystone Center is organizing a Scientist to Scientist Colloquium for 1993. We hope to have an event that equals, if not surpasses, our past successes.

Robert W. Craig
President, The Keystone Center

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SESSION ONE:

THE EVOLUTION OF FORM AND FUNCTION IN MOLECULES AND ORGANISMS

SPEAKERS:

Dr. Jack W. Szostak
Harvard Medical School/Massachusetts General Hospital

Dr. Rudolf A. Raff
Indiana University

The first session of the 1992 Scientist to Scientist Colloquium was entitled "The Evolution of Form and Function in Molecules and Organisms." The topic chair, Dr. Ford Doolittle of Dalhousie University, introduced the participants to the field of evolution by outlining some of the critical concepts that underlie the presentations of the two speakers who followed.

The first speaker was Dr. Jack Szostak, a professor of genetics at Harvard Medical School and Massachusetts General Hospital. Dr. Szostak's current work essentially focuses on the origin of life. He is trying to simulate the development of the earliest living cells in his laboratory. He is not looking to create a computer model or a machine, but is trying to create an extremely simple cell that has the ability to replicate and evolve.

Dr. Szostak explained that until ten years ago, molecular biologists knew of no molecule in which both phenotype and genotype were expressed. Such a molecule would contain the essential information needed for replication, evolution, and essentially, life. A monumental breakthrough was the discovery of an RNA molecule that also acted as an enzyme. This breakthrough allowed Dr. Szostak and others to construct theories and run experiments that investigate how this molecule could replicate and evolve.

Dr. Szostak walked the participants through the chemical processes that could transform simple sugars and amino acids into single-stranded and double-stranded RNA molecules. As this process is repeated many times, some random sequences are created that enable an RNA double-stranded molecule to separate and replicate its complement. Dr. Szostak explained that if this RNA is contained within a membrane, it will continue to replicate itself, forming a feedback loop. The RNA molecules that replicate themselves most efficiently, therefore, will have a reproductive and evolutionary advantage. This is the beginning of evolution.

The concept of this development is straightforward relative to figuring out how to reconstruct this process in the lab. Dr. Szostak showed participants how he is attacking the problems of identifying RNA molecules that have the ability to replicate, how these molecules are isolated, and how he is introducing mutations and isolating ever more efficient replicators.

The discussion that followed the presentation touched on two main questions. What is the nature of the dividing line between what is life and evolution and what is merely chemistry? Also, does the single genetic code present today indicate that all living cells evolved from a single ancestor? The discussion not only clarified the subject matter, but also clearly demonstrated that scientists from different fields work with different sets of assumptions. At the beginning of the presentation, "evolution" meant something very different to the physicists and chemists than it did to the biologists. Dr. Szostak's clarifications and explanations showed that while these disciplinary differences in assumptions and terminology can be confusing, they are certainly not a significant barrier to communication and understanding.

The second half of the evolution session was led by Dr. Rudolf Raff, Director of the Institute for Molecular and Cellular Biology and Professor of Biology at Indiana University. Dr. Raff's presentation delved into the questions concerning how an organism develops from a fertilized egg into an adult, and specifically how body plans are created and molded.

A body plan, Dr. Raff explained, is a blueprint for a group of organisms. It is a sketch of the major structures and relationships between structures that exist within an organism. Animals that have similar body plans have been separated by taxonomists into 33 different phyla. An example of one of these body plans, the planarians, was described by Dr. Raff. All the organisms within this phylum have three cell layers, bilateral symmetry, an identifiable end, and a nervous system that runs down the body axis.

In his presentation, Dr. Raff showed that animal body plans began to appear very quickly at the beginning of the Cambrian period, roughly 550 million years ago. Since that time, no new body plans have appeared. One explanation is that the availability of empty ecological niches restricts survival of new body plans. Dr. Raff pointed out, however, that about 275 million years ago 95 percent of the species went extinct, leaving many niches unfilled. And yet no new body plans developed. This has provided evidence that the restriction on the evolution of new body plans is developmental.

At first glance, it would seem that the eggs of different organisms are very similar and that as they develop into adults, their morphological similarities would gradually decrease. Contrary to this fan-like vision of development, the reality seems to be an hourglass procession of development from egg to adult. There is a diversity in the early developmental modes and early on there is a certain amount of freedom to evolve. At some midpoint, however, there is an evolutionary constrained pattern of development and the evolution of many organisms seems to converge. Later in development, organisms are again free to evolve and the similarities noticed at the bottleneck slowly disappear.

Although much is still unknown about the mechanisms that control these processes, Dr. Raff feels that he is beginning to answer some basic questions. His experiments indicate that a global information system probably controls early embryonic development. Later in the development of the embryo, evolution seems to work in domains within the embryo, which have been partitioned and insulated from other areas. The counter-intuitive middle stage of development, at the narrow neck of the hourglass, is especially intriguing. At this stage evolution and development apparently act at both levels. The same information seems to be directing events at both the global and specific levels, in a highly interactive way.

Many of the participants were intrigued by the mystery of the lack of new body plans. To many it seemed as though evolution has been frozen. The resulting discussion revolved around how this could have happened. Dr. Raff explained that once he and his co-workers more fully understand the processes of development and what exactly is happening, this will ultimately lead to discovering the mechanisms controlling this development and lead closer to the answers to the participants' questions.

SESSION TWO:
HIGH PRECISION PHYSICS

SPEAKERS:

Dr. William D. Phillips
National Institute of Standards and Technology

Dr. Clifford M. Will
Washington University

The subject of the Colloquium's second session was "High Precision Physics." **Dr. Norman Ramsey**, Nobel Laureate and Professor of Physics-Emeritus from Harvard University, acted as topic chair and gave a brief history of what types of measurements are considered high precision and the practical uses of some of these measurements.

Although there are many different types of high precision measurements, the first speaker, **Dr. William Phillips** from the National Institute of Standards and Technology, focused on measurements of frequency or time, the most accurately measurable physical quantities. As one example he described the measurement of the ratio of the magnetic moment of the proton in water to the magnetic moment of the electron in hydrogen. After explaining his experiment in detail, Dr. Phillips told the participants that the resulting value was accurate to 10^{-8} . This level of accuracy was a great improvement on past measurements.

Dr. Phillips argues that the precise measurement of such seemingly arcane quantities is crucial to the investigation of the physical world. When the ratio of magnetic moments is combined with a number of other quantities, a constant called the fine structure constant can be calculated. The fine structure constant is a measure of the charge of an electron and is used to calculate electromagnetic interactions. It turns out that the level of accuracy Dr. Phillips achieved in 1975 was critical to a definitive test, completed just a few years ago, of our basic understanding of these interactions.

Precise frequency measurements can also be used to search for a possible electric dipole moment (an uneven distribution of electric charge) on a simple object such as an atom. While many theories predict such a moment, to date, measurements have shown that if an electric dipole moment exists, the displacement of the uneven charge is less than 10^{-26} centimeters. As the measurements have gotten more accurate, theories predicting a relatively large electric dipole moment have been discredited. Once the measurement gets accurate enough to detect a permanent electric dipole moment, this will then give physicists a clue to a larger issue - why the laws of nature are not the same if the direction of time is reversed.

In the last section of his presentation, Dr. Phillips outlined how high precision measurements have contributed to present technology. In particular, he focused on the construction and uses of the atomic clock, which in itself is a high precision measurer of time. Dr. Phillips and others have developed techniques that use lasers to trap and hold individual atoms. These techniques are now being applied to make atomic clocks that may be 100 times more accurate than those used today. Already this technology is expanding into biology in the form of optical tweezers in which biologists can use lasers to grasp and move bacteria and organelles within tiny organisms.

Questions during the discussion period ranged from how to measure the cold temperatures of trapped atoms to the value of measuring accurately to just one more decimal place. It seemed though, regardless of discipline, all scientists were intrigued by the demands, pitfalls, and benefits of ultra-accurate measurements.

Dr. Clifford Will, professor and chairman of the Physics Department at Washington University-St. Louis, gave the second presentation of the "High Precision Physics" session and focused on the use of high precision techniques in the testing and practical application of Einstein's theory of general relativity (GR).

One of the predictions of GR is that the sun's gravity will cause light to deflect a small, but measurable amount. The discovery of quasars in the 1960s allowed the accurate measurement of the deflection of radio waves by using two radio telescopes to record the arrival of waves. Dr. Will explained that the differences between the recorded arrival times resulting from the GR light deflection are extraordinarily small (in the nanosecond and sub-nanosecond range) and could only have been detected with the advent of ultra-accurate atomic clocks. The results verify GR to one part in a thousand.

The use of binary pulsars to test GR also could not have been accomplished without an ultra-accurate measurement of time. The binary pulsar is a pair of neutron stars in a single orbit, one of which emits pulses of energy toward the earth. The energy pulses are regular, except for tiny distortions in each pulse's arrival time caused by the orbital motion, measurable only with an atomic clock. When physicists assumed that GR was in effect, three different calculations of the stars' masses agreed. Dr. Will showed that if GR had been ignored, the three results would have been contradictory. This elegant experiment both revealed the stars' masses and confirmed the theory of GR. It also revealed the existence of gravitational waves, which carry energy away from the system and cause the orbit to shrink.

Ultra-high precision is required in the many ongoing experiments designed to detect gravitational waves directly. Present gravity wave detectors have a sensitivity of 10^{-18} and can only detect the strongest gravitational waves, which cross the earth perhaps once every 30 years. There are plans to use laser interferometry to increase the sensitivity of these experiments to better than 10^{-21} . This level of accuracy will be sufficient to detect weaker gravitational waves, which cross the earth two or three times a year, allowing the emergence of a new "gravitational wave" astronomy.

Dr. Will concluded his discussion by describing a practical application of GR. The Global Positioning System (GPS) is used by the military to pinpoint a receptor's location anywhere on the surface of the earth to within 30 meters. GR predicts that clocks moving at different speeds and located at different heights in a gravitational field will run differently. As a result, atomic clocks in the GPS satellites that orbit the earth run about 40,000 nanoseconds faster per day than clocks on earth. The 30-meter error allowance corresponds to a 100 nanosecond difference between the satellites' and the earth's clocks. Therefore, only by using ultra-accurate atomic clocks and accounting for the effects of GR can the military operate a system that will fit their needs.

The questions during the discussion period mainly concerned the intricacies of GR, but evolved into a vigorous discussion of the allocation of funding for large versus small physics projects.

SESSION THREE:

CHEMISTRY

SPEAKERS:

Dr. Steven G. Boxer
Stanford University

Dr. Graham R. Fleming
University of Chicago

The third session of the Scientist to Scientist Colloquium was broadly entitled "Chemistry." The session's topic chair, **Dr. John Brauman**, the Jackson-Wood Professor of Chemistry at Stanford University, narrowed the session's focus by choosing two speakers, one who studies ultrafast reactions in photosynthesis and one who is developing techniques in ultrafast spectroscopy. Although these two chemists are pursuing very different subjects within their discipline, the common thread that linked the two was the understanding and potential use of ultrafast reactions.

The first speaker, **Dr. Steven Boxer**, Professor of Chemistry at Stanford University, focused his presentation on introducing the participants to the structures and mechanisms involved in electron transfer reactions in photosynthesis. Dr. Boxer explained that since these reactions are ultimately responsible for all naturally stored energy, understanding this system in detail has significant consequences for agriculture, energy, and the environment.

The system in which the electron transfer reactions take place is complex. In plants and in some bacteria, chlorophyll molecules are held in a matrix and act as an antenna array. This antenna-like structure gathers energy from the photons that strike the chlorophyll molecules and funnel it into a specific trans-membrane protein called a reaction center (RC). The RC protein is only one of two trans-membrane proteins that has ever been crystallized and whose molecular structure has been determined. Only this detailed structural knowledge enables chemists to investigate the individual steps involved in electron transfer reactions.

Dr. Boxer explained that three major observations of the RC remain unresolved. First, electron transfer happens extremely quickly, possibly faster than 1 picosecond (10^{-12} seconds). This reaction is among the fastest, well-characterized reactions in any system. Why does it have to be so fast? Second, the rate of initial electron transfer reactions actually increases as the temperature is lowered, even to such extremely low temperatures as 1.2 degrees Kelvin. Third, the RC structure has a high degree of symmetry and it seems as though two electron transfer pathways are available. Yet electrons during the transfer process always travel along a single path. A final area discussed concerned how the electron transfer reactions are affected by both external and internal electric fields. Dr. Boxer outlined what is presently being done to clarify all of these questions.

Participant questions addressed the function of the electron transfer system as well as broader areas such as the evolution of the transfer system and the nature of the antenna array of chlorophyll molecules. The interest of the participants demonstrated what Dr. Boxer said in his presentation, "The molecular basis of RC function is a problem at the intersection of many fields of science and is a rich area for exploration."

Dr. Graham Fleming, the Arthur Holly Distinguished Service Professor at the University of Chicago, was the second speaker of the chemistry session. In his presentation, Dr. Fleming introduced the Colloquium participants to some of the central ideas involved in the microscopic control of molecules and described some of the technical developments that are going on in ultrafast spectroscopy that may allow these techniques to be implemented.

Dr. Fleming explained that for a long time chemists have been manipulating molecular reactions in order to create desirable products. Today, as in the past, this is done by starting a reaction and letting it take its course. The reaction can be slightly modified by changing the outside conditions, but results are often inefficient and many byproducts are produced. Ideally, chemists would like to have microscopic control of the molecules with which they work. They would love to have the ability to select and break individual bonds, thereby creating the exact molecule that they want to use or produce. One proposal to gain this control concerns the use of ultrashort pulses of light to transfer energy into a particular bond to break it.

Since the development of flash photolysis in 1949, scientists have gradually been able to develop shorter and shorter pulses of light. The briefest pulse of light that scientists can now create is approximately 5 femtoseconds. These are remarkably small time scales. The pulses of light must be incredibly brief in order to apply energy into a bond faster than it takes for that energy to diffuse throughout the molecule. Energy applied in such a way creates vibrational "wave packets" between the nuclei held in the bond. If this can be done, then one can visualize the application of multiple light pulses, coordinated so that there is constructive interference, and the vibrational motion is increased until the bond breaks. All of this would have to be done extremely quickly, before the energy had a chance to diffuse.

Dr. Fleming pointed out that this process has only been studied by modelling the system on a computer. Many hurdles prevent the immediate implementation of these schemes, but there has been progress. Advances in understanding this chaotic system have been made by using optimal control theory, which lets one work backwards from an ideal solution and determine the steps that need to be taken to achieve it. Another obstacle to the development of this type of exact control has been addressed by Dr. Fleming and his laboratory at the University of Chicago. They have developed a method for setting and maintaining the relative phases of the ultrafast pulses. If the light pulses cannot be exquisitely controlled, the process cannot be performed.

Although this subject was highly technical, it was made accessible to all the Colloquium participants from the various disciplines. Participants questioned Dr. Fleming as to the potential application of this technique and to the present status of its development. Many felt that it was thrilling to hear of such a cutting-edge development while it is still in its infancy.

SESSION FOUR:
MANAGING SCIENCE: WHAT WORKS?

SPEAKERS:

Dr. Michael Telson
U.S. House Committee on the Budget

Mr. William A. Stiles
U.S. House Committee on Science, Space, and Technology

Of the seven sessions presented at the Colloquium, six dealt with specific scientific disciplines. The goal of the only nonscience-oriented session, "Managing Science: What Works?," was to provide the participants with a view on science funding and policy issues from the perspective of the House of Representatives. The topic chair of the session, **Dr. Daniel Kevles**, the Koepfli Professor of the Humanities at the California Institute of Technology, provided an historical background of the ebb and flow of congressional interest in science and the willingness of Congress to fund science programs.

Following this introduction, **Dr. Michael Telson**, Senior Analyst for the U.S. House Committee on the Budget, explained to the participants how the national budget is developed and how funding for science programs is considered as the budget evolves. He also described the financial pressures that are affecting federally supported science in fiscal 1993. The resulting discussion focused on how scientists and the scientific community can participate in this process.

Dr. Telson showed in detail how the budget process progresses from the submission of the president's budget through the allocation of funds to and within each congressional committee and ending with the passing of the 13 individual appropriation bills. He emphasized that the most important stage of the process for science and science funding comes just after the Appropriations Committee has been allotted its share of funds. It is the Appropriations Committee that reserves a portion of its money for the HUD/VA subcommittee for example, which, in turn, allocates these funds to NSF, NASA, and other science-oriented agencies.

But it isn't quite this straightforward. Dr. Telson emphasized that the fiscal 1993 budget is under enormous financial stress. He showed participants that the combined effect of three factors has resulted in the constriction of funds available for domestic discretionary programs (which include all science agencies except for the defense and internationally related ones). These factors are: long-term funding commitments from the 1980s (including increased entitlement spending), the necessity of financing an enormous national debt, and temporary legal barriers that prevent funds from being transferred between three major budget subdivisions (Domestic, International, and Defense). The result is that domestic discretionary programs as a whole must take at least a 1.3 percent cut in aggregate. If new programs are developed or if budgets for some programs are increased, then other programs must make up the difference and make deeper cuts.

The theme of the following discussion seemed to be whether or not the scientific community should lobby Congress and how they can do this. One scientist felt that lobbying was not appropriate since the scientific community is working for the good of society, for the progress of knowledge, and not for the self-interests of the individuals. In Dr. Telson's opinion it is the responsibility of the scientific community to communicate (not lobby) their needs, their successes, and their visions. Only in this way can they protect or enhance their reputation as a worthy endeavor, especially in these difficult economic times.

In contrast to Dr. Telson's explanation of the budget process, Mr. William Stiles, the Legislative Director of the House Committee on Science, Space, and Technology, concentrated on describing the evolution of Congress's perception of science, the scientific community, and science funding over the past 50 years.

Mr. Stiles pointed out that in 1945, when Vannevar Bush gave his landmark speech on the compact between science and society, the faith in science and new technology was at an all-time high. The result was an enormous, almost blind investment into industrial and defense-related science. The economy of the United States was the only industrial complex to escape the war's ravages and combined with the scientific investments, it would dominate the world over the next 20 years.

But during the seventies, attitudes toward science and its products began to change. Mr. Stiles mentioned that debates over SST, nuclear power, environmentalism, and animal welfare are indicative of this transition. The public no longer accepted scientific products without reservation or objection. The recent developments in biotechnology and recombinant DNA are contemporary examples. Even when scientists publicly aired their concerns and developed an open process to deal with societal concerns on this issue, much of the publicized reaction was negative. In short, Mr. Stiles feels that the chaste and special relationship science had experienced during the post-war era has eroded.

Mr. Stiles pointed out that this is in no way a decay of science itself, but a decay of the perception of science. He also gave examples of this decay in Congress. As the budgetary restrictions grow, science, like all other areas, is becoming increasingly scrutinized. Investigations into overhead expenses, inquiries into scientific misconduct, and demands that science justify the funds that have been and will be committed in the future have increased.

What can the scientific community do to reverse this degeneration of trust? In the second half of his presentation, Mr. Stiles emphasized that the scientific community must educate the Congress as to the value of what science has accomplished and its possibilities for the future. He stressed that congressmen are most attentive to their constituents. Institutions of higher learning exist in almost every congressional district and so communication at the district level is the key to communicating with Congress.

The ensuing discussion went on for over an hour. Mr. Stiles and Dr. Telson fielded questions that dealt with all facets of the relationship between the scientific community and Congress. Participants asked for examples of how to go about educating congressmen and asked how Mr. Stiles felt Congress must adapt. In fact, adaptation was an important theme. Although the scientific community can take steps to avert the further erosion of the compact between science and society, the times have definitely changed and so has the nature of this compact.

SESSION FIVE:

ASTROPHYSICS: VIEWS OF THE UNIVERSE

SPEAKERS:

Dr. John C. Mather
NASA, Goddard Space Center

Dr. Stephen Shectman
The Observatories of the Carnegie Institution of Washington

The evening of the Colloquium's fourth day was devoted to astrophysics. Dr. Margaret Geller of the Harvard-Smithsonian Center for Astrophysics chaired the session and chose Dr. John Mather, from NASA's Goddard Space Center as the first speaker.

Dr. Mather is the Project Scientist for the Cosmic Background Explorer (COBE) satellite and the Principal Investigator for the Far Infrared Absolute Spectrophotometer (FIRAS) experiment, one of three experiments that COBE carries. The goal of the FIRAS experiment is to measure the spectrum of the cosmic background radiation and compare the results to the predictions of the Big Bang theory. Before jumping into the early results of the FIRAS experiment, Dr. Mather gave Colloquium participants a brief explanation of how astrophysicists presently view the universe.

Today, astrophysicists know that the universe is expanding. This expansion was predicted by general relativity, but the first observational confirmation came in 1929. Dr. Mather explained that at that time, Edwin Hubble observed that distant galaxies seemed to be receding and that the furthest galaxies were receding faster than the closer, brighter galaxies. It was hypothesized that an explosion, a "Big Bang," had occurred and caused the universe to begin to expand.

The universe is still expanding, but what scientists do not know is which of three possible fates await it. Will the expansion slow down, stop, and will the universe then begin to collapse? Will the expansion slow down and reach a velocity of zero at some infinite time? Or will the expansion of the universe continue forever? If the acceleration or deceleration of the universe could be measured, then the fate of the universe might be determined. Unfortunately, the accuracy needed to measure the changes in velocity of a galaxy that would indicate acceleration or deceleration is not available. Although exactly how the universe is expanding is still unknown, the Big Bang theory is well accepted by astrophysicists.

One of the predictions of the Big Bang theory is that background microwave radiation would be left over from the initial explosion. This radiation was first detected in the 1960s, but until Dr. Mather's FIRAS experiment, its spectrum had not been measured. Preliminary data from FIRAS indicate that the spectrum is in accordance with what is predicted by the Big Bang theory, thereby adding to the strength of the theory's credibility.

Dr. Mather took great care to explain the design and intricacies of all three experiments that are attached to the COBE satellite. As a result, many of the questions in the discussion addressed the experimental results and the type of statistics used to interpret the data rather than the technique. Dr. Mather explained that these results will be augmented by many more months, and in some case years, of data. He is sure that as the experiments continue, the snapshot of the early universe will continue to emerge and scientists will develop an increasingly clearer view of the early universe's form and evolution.

While Dr. Mather's discussion described experiments that try to catch a glimpse of the early form of the universe, Dr. Stephen Shectman, an Astronomer at the Observatories of the Carnegie Institution of Washington, explained how he wants to develop a better view of today's universe. Dr. Shectman hopes to answer three questions that face astronomy. How much matter is in the universe, how did it get where it is, and specifically where is it?

A possible approach to the first question is to try to determine the mass that exists in a smaller, but representative, volume and extrapolate that result to the universe as a whole. A possible approach to the second question might be to use the known physical laws and, as Dr. Shectman said, "run the film backwards" to find out where the mass might have been at early times. But both of these approaches rely on knowing the location of the universe's mass, or at least part of it. That, in essence, is Dr. Shectman's third question, "Where is the mass?" It is his approach to this question that he discussed with the Colloquium participants.

Dr. Shectman explained that in the 1920s, Edwin Hubble confirmed that the universe is expanding. Since the volume of the universe is expanding, everything within the universe is getting further apart. When this is observed from earth, it seems as though everything is rushing away. Those galaxies that are furthest away in absolute terms are actually moving away the fastest. It turns out that the redshifts (the change in perceived frequency of light waves due to movement toward or away from the observer) of the galaxies can be measured by examining a galaxy's spectrum. From this information the distance to a given galaxy can be calculated.

Until recently, detailed maps of the universe's galaxies were two-dimensional. Dr. Shectman, Dr. Geller, and others are now measuring the redshifts of many galaxies and are beginning to create a three-dimensional map of the heavens. Dr. Shectman told participants that in the beginning, measuring redshifts of galaxies was a long and tedious process. A telescope would have to be trained on a single galaxy for a few hours in order to measure its spectrum. Dr. Shectman has developed a technique that allows hundreds of redshifts to be measured every two hours. Hundreds of optical fibers are connected to a single telescope and arranged so that each fiber is aligned with a single galaxy. A spectrum for each galaxy can be recorded and their redshifts calculated. The result is a redshift survey and the three-dimensional locations of a known sample of galaxies.

Although Dr. Shectman does not fully understand the distribution of mass within the universe, his present pursuit of an extensive redshift survey is an important first step toward gaining that knowledge. Discussion focused on how Dr. Shectman's early data can be interpreted and how it can be applied to larger questions such as the universe's rate of expansion and the physical parameters during the Big Bang. Without a doubt, the participants were thrilled by a science that not only gave them a sketch of our universe, but an insight into its past and future.

SESSION SIX:

THE IMMUNE SYSTEM: OUR BODY'S DEFENSE DEPARTMENT

SPEAKERS:

**Dr. David Baltimore
Rockefeller University**

**Dr. Leroy Hood
University of Washington**

**Dr. Irving L. Weissman
Stanford University School of Medicine**

The Colloquium's session on immunology was entitled "The Immune System: Our Body's Defense Department." **Dr. David Baltimore**, a professor at Rockefeller University and a Nobel Laureate, was the session's topic chair and the first of three speakers. Dr. Baltimore's presentation outlining the basic parts and functions of the immune system served as background for the more specialized presentations that followed.

Dr. Baltimore explained that the immune system is decentralized. The bone marrow, the thymus, lymph nodes, tonsils, and Peyer's patches are all part of the immune system and are not found in single location. They are located at the primary entrances and pathways that foreign invaders (antigens) use to attack the body. All of these organs sample the blood and the lymph systems in order to identify antigens and ultimately destroy them. Antigens can be viruses, bacteria, protozoa, fungi, or multi-cellular parasites. The basic tool the immune system uses for the identification of these organisms is the antibody.

An antibody is a molecule that physically binds to antigens and marks them for destruction by other parts of the immune system. Cells of the immune system, called B cells, each produce an antibody on their cell surfaces. Each B cell produces a different antibody, the structure of which is so specific that any given antibody will bind tightly to only one antigen.

Dr. Baltimore showed the Colloquium participants that once an antigen is bound to one of these antibodies, the B cell reacts by rapidly reproducing and shifting its function to the mass production of identical, but unattached, antibodies. These antibodies are allowed to circulate through the blood and lymph systems and bind to identical antigens that have infected the body. Other cells of the immune system, phagocytes, attack the bound antigens and destroy them. A third kind of cell, the T cell, both helps the B cell to produce antibodies and can directly kill cells that harbor an infectious agent.

But, Dr. Baltimore pointed out, the immune system is vulnerable. There are diseases that attack the immune system itself. Leukemia and lymphoma are cancers in which cells of the immune system grow out of control either in the blood or in solid masses. The immune system also malfunctions. Allergies are a result of the overreaction of the immune system to a variety of protein antigens. Other maladies, such as rheumatoid arthritis, can be caused by the immune system attacking the body's own cells.

Following Dr. Baltimore's presentation, a wide-ranging discussion developed. Among other topics, many of the participants wanted to know more about exactly how the immune system distinguishes between foreign invaders and the body's own cells. These issues naturally led Dr. Baltimore to move on and introduce the session's second speaker.

Dr. Leroy Hood, Professor and Chairman of the Department of Molecular Biotechnology at the University of Washington, followed Dr. Baltimore's broad introduction to immunology with a molecular view of immunology. He focused on the dual need for the immune system to both aggressively attack foreign cells (non-self) and be tolerant of the body's own cells (self). The key to the system is the process of recognition.

Dr. Hood explained to the participants exactly how elements of the immune system interact during the recognition of antigens. The basic idea is that foreign protein fragments are presented to specialized immune cells, called T cells. The T cell will "recognize" the foreign fragments (antigens) and instruct the immune system to attack cells that include this protein, wherever they find them.

But how does a T cell distinguish between self and non-self proteins? Dr. Hood outlined an elegant two-stage process that screens all of the body's T cells and selects only those cells that fail to recognize self. T cells that recognize self are destroyed. In some people, however, not all the T cells that recognize self are destroyed. These people can develop what is termed an auto-immune disease. One example given by Dr. Hood was multiple sclerosis (MS). This disease is the result of the immune system recognizing and slowly destroying the protein found in the myelin sheath that surrounds nerves and helps propagate electrical impulses.

Using MS as an example, Dr. Hood explained that immunologists have been able to develop animal models to study the intricacies of autoimmune diseases. By using techniques developed in molecular biology, immunologists have both simply induced MS symptoms in mice and have also manipulated the mouse immune system so that mouse T cells spontaneously recognize and attack myelin proteins, presumably how it happens in humans. From these models, particular T cells and important molecules have been identified that, if present, predispose a mouse to MS.

Dr. Hood and his colleagues have developed techniques that prevent and, in some cases, reverse MS in the mice models of the disease. This has been possible by permanently eliminating the specific T cells that recognize the myelin protein or by disabling the molecules that present the protein fragments to the T cells. Dr. Hood pointed out that although these techniques work to stop mouse MS, both techniques inhibit the general efficiency of the immune system and may make the mouse more susceptible to other diseases.

During his presentation, Dr. Hood also discussed how this technology might be extended to the treatment of human autoimmune diseases as well as how the immune system may have evolved.

The final presentation of the Colloquium's session on immunology was given by **Dr. Irving Weissman**, Professor of Pathology at Stanford University School of Medicine. In contrast to the molecular view given by Dr. Hood, Dr. Weissman presented a cellular view of the immune system and explained how it seems to function in the body.

Dr. Weissman pointed out that modern studies of immunology first developed during the 1940s and 1950s as scientists began to use radiation as a tool to manipulate and examine the immune system. Experiments have shown that mice given a lethal dose of radiation can be saved if given an injection of bone marrow from a blood-forming and genetically similar mouse. It was determined through the use of genetic markers that an entirely new blood-immune system develops in the mouse. Using antibodies and techniques developed in molecular biology, researchers have been able to determine which cells are responsible for this rejuvenation. Essentially, researchers sifted through bone marrow samples and removed all cells that they knew to have specific blood or immune functions. The remaining cells were then selectively sorted. After this process, only 1 in 2,000 cells remained with reconstitutive activity. These cells are stem cells.

Stem cells, Dr. Weissman showed, are extraordinary. Under the correct conditions, they not only have the ability to reproduce (self-renew), but also to differentiate into the various types of specialized cells found in the immune and blood-forming systems. In fact, an injection of 100 stem cells into a mouse whose immune system has been destroyed by radiation can be enough to reconstruct an entire, functional immune system. Another experiment, also using genetic markers, demonstrated that all cell types found in the immune and blood systems can actually develop from a single stem cell.

After taking the participants through the series of experiments that demonstrated how the immune system develops *in vivo*, Dr. Weissman discussed what ramifications this knowledge may have on humans. Researchers have thought of potential therapies that use stem cells to cure leukemia, methods that could solve the graft versus host disease that complicates organ transplants, and therapies that could potentially cure AIDS. The possibilities are endless, but Dr. Weissman felt that there is still much to be learned about the immune system and that many obstacles must be overcome before any of these theories can be thoroughly investigated.

Participants' questions touched on many different areas of immunology. Some wanted to know the current status of the use of fetal tissue in the kinds of experiments Dr. Weissman described. Others wanted to know more about the precursors and development of stem cells. However, virtually every Colloquium participant felt that a science with a reputation for complexity was made quite a bit clearer by three of its most accomplished practitioners. The discussion after all three presentations demonstrated that this science is accessible to the nonbiologist and is incredibly intriguing to scientists as a whole.

SESSION SEVEN:
COMPUTER SCIENCE

SPEAKERS:

Dr. Rodney A. Brooks
Massachusetts Institute of Technology

Dr. W. Daniel Hillis
Thinking Machines Corporation

The final session of the 1992 Scientist to Scientist Colloquium was broadly titled "Computer Science." The topic chair was **Dr. Edward Feigenbaum**, a professor in the Computer Science Department at Stanford University. To begin the session, Dr. Feigenbaum gave participants an introduction to the evolution of computers and computational theory. In particular, he outlined the classical approach that many in computer science have taken when studying and trying to create artificial intelligence (AI). This provided a background for the two speakers who followed.

The first speaker was **Dr. Rodney Brooks**, an Associate Professor at the Artificial Intelligence Laboratory at the Massachusetts Institute of Technology. First, Dr. Brooks described some of the formal methods that result from thinking about AI and specifically how they relate to robotics.

Classically, the first step in trying to create AI is to have a robot examine its environment. The robot would then use incoming data to build a model of its environment by converting the information into logical statements. Referring to this model, a robot would select a sequence of actions that allow the robot to locomote successfully. Finally, some type of motor control system would carry out the appropriate mechanical actions.

Up through the 1980s, AI specialists believed that they might be able to create an intelligent system if they refined each of these separate steps. Around this time, Dr. Brooks and others found that the separate pieces people had been designing did not complement each other and that enormous amounts of computation were needed in order to make them function. Their reaction has been to ignore the classical dogma and formal methods of AI and, in the case of Dr. Brooks, to examine simple biological systems for new clues.

Dr. Brooks explained to the participants that he was inspired by how insects seemed to function. Thus motivated, he created a robot that could attain the simple goal of walking. By adding extra functional "layers," one by one, the robot was gradually able to do more complicated things. "Locomotion" was the initial layer. "When hitting something, try to climb" was a second layer. Each additional layer acted in parallel to the previous layers, yet each influenced all other layers by promoting or inhibiting reactions to particular sensed events. The important departure of this approach from AI dogma is that there was no internal representation of the external world.

Dr. Brooks' approach to robotics and AI has ignored the conventional wisdom of AI dogma. By examining simple biological systems, he has been able to create a functional robot that seems to have some aspects of intelligence. During the discussion period, most Colloquium participants seemed to be intrigued by the idea of relating the function of Dr. Brooks' robots to the behavior displayed in nature by insects and small animals. This interest in the interface between aspects of computer science and nature carried into the session's second presentation.

Dr. Daniel Hillis is the Chief Scientist at Thinking Machines Corporation in Cambridge, Massachusetts, and was the second speaker at the Colloquium's session on computer science. In introducing his presentation, Dr. Hillis said, "If I had another fifteen minutes, I think I could send you all away knowing how to design a computer. And we will come very close to that anyway." In his forty-five minute presentation, Dr. Hillis explained the Boolean laws that are the basis of processing information in computers, how conventional computers are designed and function, and a new approach to computing that he has pioneered - parallel computing.

The Boolean laws of thought is a type of algebra whose variables can have values of true or false. Dr. Hillis gave this example of Boolean logic: If A is true or B is true, then the assertion that A is false and B is false, is false. Boolean logic can be represented in switching circuits by having electric current open or close switches. If the switches are closed, this may denote true. If switches are open, this would then denote false. Dr. Hillis took participants through a detailed example of how these individual circuits can be combined to perform specific computational procedures.

Dr. Hillis also explained how a finite number of these circuits can be used to create a Turing Machine, which, given the correct input, can compute any conceivable function. This machine is absolutely universal and most of today's computers are based on this scheme. Today's computers have the same design as early computers, but they have been given more circuits (memory), have been miniaturized, and have been speeded up. Yet the basic design has not changed.

Approaching computer design and artificial intelligence through problems associated with image processing, Dr. Hillis felt the conventional scheme was inadequate. Humans process images very quickly, yet the brain has less memory and operates relatively slowly compared to modern computer systems. His solution was to build a computer that uses thousands of small processor-memory combinations connected to each other through a communication system. Each of these small units process some part of the data, all working simultaneously. This parallel computing machine solved some of the problems associated with the manipulation of incredibly large amounts of data, but did not solve other questions concerning AI.

As a conclusion, Dr. Hillis described his present efforts to develop new approaches to computer science through a process analogous to evolution. In short, a computer program is allowed to evolve "in computo." The computer selects and propagates those programs that, for example, may sort numbers efficiently. After thousands of generations a program is produced that does the specified task extremely well. Dr. Hillis explained that since the brain has undergone significant evolutionary pressures and is quite advanced, then the same process may take computers one step closer to AI. As with Dr. Brooks' presentation, participants concentrated their questions and remarks on the biological and evolutionary perspectives found in this growing science.

APPENDIX A:

BIOGRAPHICAL SKETCHES OF COLLOQUIUM SPEAKERS

DR. DAVID BALTIMORE

Dr. David Baltimore is a leader and spokesperson for science on many issues, including genetic research, priorities for national research, and matters of international concern, such as biological warfare and the regulation of science. In 1986, he was appointed co-chairman of a major study of AIDS, sponsored by the National Academy of Sciences and the Institute of Medicine. He continues in that position and also served on the AIDS Oversight Committee of the Institute of Medicine.

In 1975, at the age of 37, Dr. Baltimore became one of the youngest recipients of the Nobel Prize in Physiology or Medicine. He shared the prize with Dr. Howard Temin of the University of Wisconsin and Dr. Renato Dulbecco of the Salk Institute for "discoveries concerning the interaction between tumor viruses and the genetic material of the cell." In 1970, simultaneously with Dr. Temin, he had discovered the enzyme, reverse transcriptase, an enzyme that enables cancer-inducing RNA viruses to replicate within the host organism. The enzyme also made possible much of the genetic research that was to follow, and its presence in the human immunodeficiency virus allowed the cause of AIDS to be uncovered. Dr. Baltimore has also received the Warren Triennial Prize from Massachusetts General Hospital, the Eli Lilly and Company Award in Microbiology and Immunology, the National Academy of Sciences/United States Steel Foundation Award in Molecular Biology, and the Gairdner Foundation Annual Award, among others.

Dr. Baltimore was elected to the National Academy of Sciences and the American Academy of Arts and Sciences in 1974 and was appointed to the Pontifical Academy of Sciences, an international body of distinguished scientists, in 1978. He is also an elected Fellow to the Royal Society (England), and in 1988 he was elected to membership in the Institute of Medicine.

Research in Dr. Baltimore's laboratory covers three areas: cancer-inducing viruses, the immune system, and infectious diseases. In each of these fields, the investigations are directed toward defining the biochemical events underlying changes in gene expression and gene structure in the mammalian cell. Work on cancer-inducing viruses has focused on one virus - Abelson mouse leukemia virus - trying to determine how the viral oncogene transforms normal cells into tumor cells. Much of his research in the immune system concerns molecular events occurring during various stages of development of antibody-producing lymphoid cells. His investigations of infectious diseases center on two viruses, poliovirus and human immunodeficiency virus (HIV). Poliovirus has been a cornerstone of Dr. Baltimore's research effort for two decades. Progress has been achieved toward a biochemical understanding of poliovirus replication in host cells and on the development of poliovirus genetics. In response to the AIDS epidemic, a growing interest has been the human immunodeficiency virus that causes the disease.

In 1960, after receiving his B.A. degree with high honors in chemistry from Swarthmore College, Dr. Baltimore began graduate studies at Massachusetts Institute of Technology. A year later he went to the Rockefeller University, from which he received the Ph.D. degree in biology in 1964. He was a postdoctoral fellow at MIT in 1963 and 1964 and at Albert Einstein College of Medicine in 1964 and 1965. He became a research associate at the Salk Institute in 1964. He returned to MIT in 1968 as associate professor, became professor of biology in 1972, and was appointed American Cancer Society Research Professor in 1973. The following year, he joined the staff of the MIT Center for Cancer Research. In 1982, he was named the first Director of the Whitehead Institute. He became President of the Rockefeller University in July 1990, and resigned from that position in December 1991, remaining on the faculty.

Dr. Baltimore is a member of the Board of Governors of the Weizmann Institute of Science in Israel and is the former Chairman of the Board of Trustees of the Scientists' Institute for Public Information.

DR. STEVEN G. BOXER

Steven G. Boxer
Department of Chemistry
Stanford University
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EDUCATION

University of Chicago
Degree: Ph.D. December 1976
Field: Physical and Physical-organic Chemistry
Research Advisor: Professor Gerhard L. Closs

Tufts University
Degree: B.S. (honors-June 1969)
Major: Chemistry

HONORS

Atomic Energy Commission Pre-doctoral Fellow (1972-1976)
Alfred P. Sloan Foundation Fellow (1979-1983)
Camille and Henry Dreyfus Teacher-Scholar Fellow (1980-1985)
Dean's Award for Distinguished Teaching (1982)
Presidential Young Investigator Award (1984-1989)
American Society for Photobiology Research Award (1992)

EMPLOYMENT

September 1988 to present	Chair, Stanford Biophysics Program
September 1986 to present	Professor of Chemistry, Stanford University
September 1982 to August 1986	Associate Professor of Chemistry, Stanford University
December 1976 to August 1982	Assistant Professor of Chemistry, Stanford University

RESEARCH INTERESTS Physical and Biophysical chemistry, photosynthesis, electron transfer, electric and magnetic field effects, protein electrostatics and dynamics, Stark spectroscopy.

DR. RODNEY A. BROOKS

Professor Rodney Brooks joined the Massachusetts Institute of Technology as a faculty member in Electrical Engineering and Computer Science, and at the Artificial Intelligence Laboratory in 1984. He had previously been a faculty member at Stanford University and a Research Scientist at both MIT and Carnegie Mellon University. His research has ranged over model-based computer vision, Lisp compilation and systems technology, automatic planning for robot assembly, mobile robot navigation, small robot technologies, and behavior-based architectures for Artificial Intelligence.

Dr. Brooks is co-founder of Lucid, Inc., of Menlo Park, California, co-founder and chairman of IS Robotics, Inc., of Westlake Village, California, and co-founder and chairman of Artificial Creatures, Inc., of Cambridge, Massachusetts. He was founding co-editor of the International Journal of Computer Vision from 1986 to 1991.

Dr. Brooks is a Founding Fellow of the American Association for Artificial Intelligence. In 1991 he was a co-winner of the Computers and Thought Prize awarded by the trustees of the International Joint Conference on Artificial Intelligence.

DR. GRAHAM R. FLEMING

Born: 3 December, 1949 - Barrow-in-Furness, England
Married: one son.

Degrees: B.Sc. University of Bristol, 1971
Ph.D. Royal Institution of Great Britain, 1974

Postdoc: Cal Tech, University of Melbourne, 1974-76

Jobs: Leverhulme Fellow, Royal Institution, 1977-79
University of Chicago, 1979 to present

Currently (since 1987) Arthur Holly Compton Distinguished Service Professor, Chairman of Department, 1988-90

Fellow: American Academy of Arts and Sciences

Scientific Interests:

- Ultrafast lasers and their use in spectroscopy.
- Dynamics of chemical processes in condensed phases.
- Molecular description of elementary photobiological processes, especially photosynthesis.
- Computer simulation of complex systems.
- Internal motions of proteins and peptides.

Book: Chemical Applications of Ultrafast Spectroscopy, Oxford University Press (1986).

DR. W. DANIEL HILLIS

Danny Hillis was born on September 25, 1956, in Baltimore, Maryland. He spent his childhood in Europe, Central Africa, Asia, and the southern United States. He entered the Massachusetts Institute of Technology as an undergraduate in 1974. As an undergraduate, Danny worked with Seymour Papert at the MIT Logo Group, developing the Logo computer language. He also worked part-time as a toy designer for the Milton-Bradley Corporation.

In 1978, he received his Bachelor's degree from MIT in the field of mathematics. He was awarded a Fannie & John Hertz Foundation Fellowship and began his graduate studies at the MIT Artificial Intelligence Laboratory. His Master's work, supervised by Marvin Minsky, was in the area of robotics. It included the development of tendon control manipulators, a touch sensitive robot skin, and algorithms for tactile recognition. He also designed a computer for playing tic-tac-toe entirely of tinker toys, which is currently in the Boston Computer Museum. His Master's degree on "Active Touch Sensing" was awarded in 1981.

During this period, Danny became interested in the physical limitations of computation and the possibility of constructing highly parallel computers. This work culminated in 1985 with the design of the parallel computer called the Connection Machine. This was the topic of his Ph.D. thesis for which Hillis won a 1985 Distinguished Thesis Award. A book based on the thesis was published by the MIT Press. His Ph.D. was awarded by MIT in 1988.

In June of 1983, Danny helped found a company, Thinking Machines Corporation, that produces the Connection Machine as a commercial product. At the company he has concentrated his research on methods of parallel programming, applications of parallel computers, and computer architecture. His current research is on evolution and parallel learning algorithms.

Dr. Hillis is the recipient of the ACM's Grace Murray Hopper Award and the Ramanujan Award. He is the holder of 17 U.S. patents and is an editor of several scientific journals, including *Complex Systems*, *ORSA Journal on Computing*, *Future Generation Computer Systems*, *Machine Vision and Applications*, and *Advances in Applied Mathematics*. He is also a member of the Science Board of the Santa Fe Institute and a Fellow of the American Academy of Arts and Sciences.

DR. LEROY HOOD

Dr. Leroy Hood is the William Gates III Professor of Molecular Biotechnology, Director of the NSF Science and Technology Center for Molecular Biotechnology, and Chairman of the Department of Molecular Biotechnology at the University of Washington School of Medicine. He has an M.D. from the Johns Hopkins Medical School and a Ph.D. in biochemistry from the California Institute of Technology. His research interests focus on the study of molecular immunology and biotechnology. His immunologic efforts have focused on a molecular analysis of the three families of immune receptors: antibodies, T-cell receptors, and molecules of the major histocompatibility complex. More recently the laboratory has focused on the molecular basis of immune recognition and autoimmune disease. His laboratory has played a major role in developing automated microchemical instrumentation that permits the highly sensitive sequence analysis of proteins and DNA and the synthesis of peptides and gene fragments. Over the past few years, he has applied his laboratory's expertise in large-scale DNA mapping and sequencing to the analysis of the human and mouse T-cell receptor loci - an important effort for the Human Genome Project.

Dr. Hood is the former Chairman of the Division of Biology (1980-1989) at the California Institute of Technology, where he was the Bowles Professor of Biology from 1977 to 1992. In addition, he was the Director of the Cancer Center at Caltech for nine years and Director of the NSF Center for Molecular Biotechnology for four years. Dr. Hood has served on the Genome Advisory Committee for both the National Institutes of Health and the Department of Energy. Dr. Hood is an editor of five professional journals. He has written more than 400 professional articles and co-authored five textbooks that cover diverse areas such as biochemistry, molecular biology, and immunology.

Dr. Hood is a member of the National Academy of Sciences and the American Association of Arts and Sciences. He received the Ricketts Medal in 1980 from the University of Chicago for outstanding contributions to biomedical research, the 3M Life Sciences Award in 1984 for significant contributions to the health and welfare of mankind, the Dickson Prize in Medicine for contributions to immunology and molecular biology, and the Albert Lasker Basic Medical Research Award for studies of immune diversity. In 1989 Dr. Hood was awarded the Commonwealth Award of Distinguished Service for work in developing instruments used to study modern biology and medicine and the Cetus Award for Biotechnology. Dr. Hood received the American College of Physicians Award in 1990 for distinguished contributions in science as related to medicine. He also holds honorary Doctor of Science degrees from Mt. Sinai School of Medicine of the City University of New York, Montana State University, the University of British Columbia, the University of Southern California, and Wesleyan University, as well as a Doctor of Human Letters honorary degree from Johns Hopkins University.

DR. JOHN C. MATHER

Dr. John C. Mather is Head of the Infrared Astrophysics Branch at NASA's Goddard Space Flight Center in Greenbelt, Maryland. He organized the first proposal for the Cosmic Background Explorer (COBE) satellite in 1974 and was appointed Study Scientist (1976) and Project Scientist (1982) for the COBE, and is Principal Investigator for the Far Infrared Absolute Spectrophotometer (FIRAS) on the COBE. He received his Ph.D. in Physics at the University of California (Berkeley) in 1974 and his B.A. in Physics with Highest Honors and Phi Beta Kappa at Swarthmore College in 1968. He is the recipient of several NASA and GSFC awards, including the John Lindsay Memorial Award from GSFC in 1990 for his work on the COBE. He also received the Rotary National Award for Space Achievement in 1991 and the National Air and Space Museum Trophy in November 1991.

DR. WILLIAM D. PHILLIPS

William D. Phillips: Born 1948. B.S., Juniata College in Physics, 1970; Ph.D., MIT, thesis under Dan Kleppner involving a precision measurement of the magnetic moment of protons in H_2O and studies of collisions between laser excited atoms; Chaim Weizmann fellow at MIT 76-78, working on spin polarized hydrogen and laser analysis of atomic collisions; 1978 joined the Electricity Division of the National Bureau of Standards in Gaithersburg, Maryland (now the National Institute of Standards and Technology) to make precision measurements of the gyromagnetic ratio of the proton and the absolute ampere, quantities of importance in determining the fundamental constants. Began a program in laser cooling of neutral atoms and formed a group, now in the Atomic Physics Division of the Physics Laboratory at NIST to study laser cooling and trapping of atoms. This group demonstrated the first laser deceleration and stopping of atomic beams, the first electromagnetic trapping of neutral atoms, and the first sub-Doppler laser cooling. Current research interests include studies of the mechanisms for laser cooling, development of new trapping techniques, quantum collective behavior of atoms, Quantum motion of optically trapped atoms, collisions and reactions between atoms at ultra-low temperature, laser cooled atomic clocks, atom optics, and manipulation of antimatter. Other appointments include visiting professorships at College de France and Ecole Normale Supérieure in Paris and adjunct professorship at the nearby University of Maryland. Member of the Optical Society of America and Fellow of the American Physical Society.

DR. RUDOLF A. RAFF

Personal:

Born Shawinigan, Que., Canada, Nov. 10, 1941
Married, two children

Education:

B.S., Pennsylvania State University, Biochemistry, 1963
Ph.D., Duke University, Biochemistry, 1967
Postdoctoral, National Naval Medical Center, Navy Active Duty, 1967-1969
Department of Biology, MIT, 1969-1971

Positions held:

Professor of Biology, Indiana University, 1971 to present
Instructor-in-Chief, Embryology Course, Marine Biological Laboratory, Woods Hole, MA
1980-1982
Director, Indiana Institute for Molecular and Cellular Biology, 1983 to present

Research interests: Evolution of processes of embryonic development, molecular phylogeny.

The fields of evolutionary biology and developmental biology have pretty much ignored each other from the end of the nineteenth century until quite recently. Consequently, these disciplines have developed very different sets of problems, methods, and terminologies. However, evolutionary transformations of morphology have to be achieved through changing the process of development in each generation. I have focused on studying the cellular and molecular mechanisms that underlie radical evolutionary changes in early development between closely related organisms that achieve the same end, but through very different courses of development.

Because much of our understanding of evolutionary relationships among animals on the very large level of phyla is based on comparative embryology, I have been reinvestigating these relationships by gene sequence data. This allows us to develop phylogenies independent of embryology against which we can test trends in the evolution of development. These studies are important in understanding the evolution of body plans.

DR. STEPHEN SHECTMAN

Steve Sheckman received his B.S. in Physics from Yale in 1969 and his Ph.D. from Caltech in 1973. He was a postdoctorate for two years at the University of Michigan, and since 1975 has been a staff member of the Observatories of the Carnegie Institution of Washington. While at Michigan he constructed the first of a series of photon-counting detectors, which were copied by several observatories around the world. Most of the galaxy redshifts that are known today have been measured with these detectors. In 1981 he and his collaborators discovered a particularly large void in the galaxy distribution, a kind of structure that has since been found to be characteristic of the way galaxies are distributed in space. Sheckman has also studied the structure of rich clusters of galaxies and is presently conducting a survey of large-scale structure using fiber optics to measure the redshifts of 100 galaxies at a time. Sheckman's other research interest has been the search for the nearly primordial stars of lowest metal abundance that were formed in the early stages of the formation of the galaxy.

MR. WILLIAM A. STILES

William A. (Skip) Stiles, Jr., is the Legislative Director for the House Science, Space, and Technology Committee. Prior to this assignment, he was Staff Director for the House Agriculture Subcommittee on Department Operations, Research, and Foreign Agriculture, a position he held in 1984 and from 1987 through 1990. Mr. Stiles has served on Capitol Hill since 1976 for Congressman George E. Brown, Jr., holding position of Legislative Assistant and Administrative Assistant in the Congressman's office.

Before working for Congress, Mr. Stiles was employed by local government in Virginia, ran a retail business, and worked for a non-profit organization. Mr. Stiles is a 1971 graduate of the College of William and Mary.

DR. JACK W. SZOSTAK

Dr. Szostak was born on November 9, 1952, in London, England. He attended McGill University in Montreal, Canada, from 1968 to 1972, where he received his B.Sc. and published his first scientific paper on the subject of the sex hormones of the colonial green algae.

His Ph.D. work (1972-1977) was carried out at Cornell University in the laboratory of Professor Ray Wu on the applications of synthetic oligonucleotides to the identification and cloning of yeast genes. His postdoctoral work was conducted in the same lab on the topic of recombination between sister chromatids in yeast.

Dr. Szostak then moved to the Dana-Farber Cancer Institute and Harvard Medical School as an Assistant Professor, where he worked on recombination and chromosome structure. His early work on recombination led to the realization that the introduction of double-strand breaks into DNA plasmids made the DNA extremely reactive, thus facilitating the recovery of yeast cells in which the transforming DNA had recombined with chromosomal DNA. This work was extended, on the basis of genetic evidence, to a general model for recombination during meiosis. Subsequent work from his and other labs has confirmed the role of double-strand breaks in normal cellular recombination. Dr. Szostak was also involved in the cloning of chromosomal elements and their assembly into the first artificial chromosomes. His lab was responsible for the cloning and characterization of telomeres from yeast and the isolation of mutants, which provided the first conceptual link between telomere integrity and senescence. The assembly of telomeres with centromeres, origins of replication, genes, and spacer DNA into artificial chromosomes provided evidence that total size was a critical parameter for highly fidelity chromosome inheritance. Yeast artificial chromosomes (YACS) have subsequently been developed in other labs as cloning vectors for large DNA fragments and are used in all of the major genome projects.

He is now Professor of Genetics at Harvard Medical School, with laboratories at Massachusetts General Hospital, Boston, Massachusetts. His current research interests are in the structure and function of RNA enzymes and the origin of life. He has published several papers on the redesign of the group I self-splicing introns into an RNA replicase, i.e., an RNA polymerase composed of RNA and capable of self-replication. Current work on the design of an RNA replicase is focused on the use of "directed evolution" experiments to isolate variant enzymes with improved catalytic efficiency, substrate binding, and accuracy of replication. Related experiments also use such evolutionary or selectionist approaches for the isolation of nucleic acid sequences with specified properties such as substrate binding and catalysis. The ultimate goal of this research is to combine RNA enzymes encoded by an RNA genome with a suitable membrane vesicle system to create a simple cell that is capable of evolving in response to natural selection.

DR. MICHAEL TELSON

Dr. Telson presently serves as a senior budget analyst with the Committee on the Budget of the U.S. House of Representatives.

Dr. Telson is responsible for advising the Committee on issues involving federal energy, science, and space programs including the Department of Energy, the NSF, and NASA. He has been with the Committee since 1975. During 1977-78, he concurrently served as staff economist to the House Ad Hoc Committee on Energy, which was created to enact President Carter's National Energy Act. During 1979-80, he concurrently served as staff coordinator for Speaker Thomas P. O'Neill's Task Force on Energy.

Dr. Telson received his Ph.D. in electrical engineering from MIT and an M.S. in Industrial Management from the MIT Sloan School of Management.

DR. IRVING L. WEISSMAN

Education:

Dartmouth College, Hanover, New Hampshire 1957-1959 (Zoology)
Montana State College (now a University), B.S. (Pre-Med) 1959-1960
Stanford University, Stanford, California, M.D. 1960-1965
Oxford University, England 1964 (Exp. Pathology)
Stanford University, Stanford, California, 1965-1967 (Postdoc)

Research and Professional Experience (all at Stanford University)

Research Associate, Department of Radiology, 7/67 - 12/68
Assistant Professor, Department of Pathology, 1/69 - 9/74
Associate Professor, Department of Pathology, 9/74 - 8/81
Professor, Department of Pathology, 9/81 - present

Awards and Honors

1986	Outstanding Investigator Award, National Institutes of Health
1987	Kaiser Award for Excellence in Preclinical Teaching
1987	Karel and Avice Beekhuis Professor of Cancer Biology
1989	Pasarow Award for Outstanding Contributions to Cancer Research
1989	Election to the National Academy of Sciences
1990	Election to the American Academy of Arts and Sciences

DR. CLIFFORD M. WILL

Clifford Martin Will is Professor and Chairman of Physics, and member of the McDonnell Center for the Space Sciences at Washington University in St. Louis. Born in Hamilton, Canada, in 1946, he received his pre-college and college education there, obtaining a B.Sc. in Applied Mathematics and Theoretical Physics from McMaster University in 1968. In 1971 he obtained a Ph.D. in Physics from the California Institute of Technology in Pasadena, and remained at Caltech for one year as an instructor in Physics. He was an Enrico Fermi Postdoctoral Fellow at the University of Chicago from 1972 to 1974. In 1974 he joined the faculty of Stanford University as an Assistant Professor of Physics and remained there until 1981. From 1975 to 1979 he was an Alfred P. Sloan Foundation Fellow, and during 1978 to 1979 he was a Mellon Foundation Junior Faculty Fellow. In 1981 he joined Washington University in St. Louis as Associate Professor, in 1985 became Professor of Physics, and in 1991, Chairman.

He has published over 125 scientific articles or abstracts, including 8 major review articles, 12 popular or semipopular articles, and two books, *Theory and Experiment in Gravitational Physics* (Cambridge University Press, 1981; 2nd edition, 1992) and *Was Einstein Right?* (Basic Books, 1986; 2nd edition, Spring 1993). The latter book won the 1987 American Institute of Physics Science Writing Award and has undergone translation into French, German, Italian, Japanese, Portuguese, Spanish, Korean, and Greek. In 1986 he was selected by the American Association of Physics Teachers to be the forty-sixth annual Richtmyer Lecturer and in 1989 he was elected a Fellow of the American Physical Society. He was Chairman of the Committee on Accuracy of Time Transfer in Satellite Systems (Air Force Studies Board, National Research Council) from 1984 to 1986 and was a Divisional Associate Editor for *Physical Review Letters* from 1989 to 1992. He is a member of the Science Coordinating Committee for Experimental Gravitation of NASA, the Committee on Fundamental Constants and Basic Standards of the National Research Council, and the Editorial Boards of *Annals of Physics* and *Classical and Quantum Gravity*.

His research interests are theoretical, encompassing the observational and astrophysical implications of Einstein's general theory of relativity, including gravitational radiation, black holes, cosmology, the physics of curved space-time, and the theoretical interpretation of experimental tests of general relativity.

APPENDIX B:
LIST OF 1992 COLLOQUIUM PARTICIPANTS

**THE 1992 SCIENTIST TO SCIENTIST COLLOQUIUM
PARTICIPANT LIST**

Dr. Eric G. Adelberger
Professor of Physics
University of Washington

Dr. Nina Agabian
Professor and Director
Intercampus Program on Molecular Parasitology
University of California at San Francisco

Dr. Berni J. Alder
Group Leader
Lawrence Livermore Laboratories
Professor
University of California at Davis

Dr. Don L. Anderson
Eleanor and John R. McMillen Professor
Seismological Laboratory
California Institute of Technology

Dr. David Baltimore
Professor
Rockefeller University

Dr. George I. Bell
Senior Fellow, Theoretical Biology and Biophysics
Los Alamos National Laboratory

Dr. Joan W. Bennett
Professor
Department of Cellular and Molecular Biology
Tulane University

Dr. William P. Bishop
Vice President for Research
Desert Research Institute

Dr. Steven G. Boxer
Professor of Chemistry
Stanford University

1992 Participant List, cont.

Dr. John I. Brauman
Jackson-Wood Professor of Chemistry
Stanford University

Dr. Rodney A. Brooks
Associate Professor
Artificial Intelligence Laboratory
Massachusetts Institute of Technology

Dr. Ronald E. Cape
Chairman
Darwin Technologies, Inc.

Dr. Paul C.W. Chu
Director
Texas Center for Superconductivity
Professor
University of Houston

Mr. Hirsh Cohen
Program Officer
Alfred P. Sloan Foundation

Mr. Robert W. Craig
President
The Keystone Center

Dr. Mark Davis
Professor of Chemical Engineering
California Institute of Technology

Dr. W. Ford Doolittle
Director, Evolutionary Biology Program
Canadian Institute for Advanced Research
Professor of Biochemistry
Dalhousie University

Dr. Darrell J. Doyle
Director
The Keystone Symposia on Molecular and Cellular Biology

1992 Participant List, cont.

Dr. Alan Dressler
Astronomer
Observatories of the Carnegie Institution of Washington

Dr. Billy Joe Evans
Professor of Chemistry
University of Michigan

Dr. Edward A. Feigenbaum
Professor
Computer Science Department
Stanford University

Dr. Graham R. Fleming
Arthur Holly Compton Distinguished Service Professor
Department of Chemistry
University of Chicago

Dr. Stephanie Forrest
Assistant Professor
Computer Science Department
University of New Mexico

Dr. L. Patrick Gage
Executive Vice President
Genetics Institute

Dr. Robert B. Gagosian
Associate Director for Research
Woods Hole Oceanographic Institute

Dr. Margaret J. Geller
Professor of Astronomy
Harvard/Smithsonian Center for Astrophysics

Dr. Ralph E. Gomory
President
Alfred P. Sloan Foundation

1992 Participant List, cont.

Ms. Susan Grether
High School Science Teacher
Polytechnic School

Dr. David Gross
Professor of Physics
Princeton University

Dr. W. Daniel Hillis
Chief Scientist
Thinking Machines Corporation

Dr. Noel W. Hinnners
Vice President and Chief Scientist
Civil Space and Communications
Martin Marietta Corporation

Dr. Leroy Hood
William Gates III Professor of Molecular Biotechnology
University of Washington
Director
NSF Science & Technology Center for Molecular Biotechnology

Dr. Alice Huang
Dean for Science
New York University

Dr. Raymond Jeanloz
Professor of Geology and Geophysics
University of California at Berkeley

Dr. Daniel J. Kevles
Koepfli Professor of the Humanities
California Institute of Technology

Dr. Susan W. Kieffer
Regents' Professor of Geology
Arizona State University

1992 Participant List, cont.

Dr. Eric S. Lander
Member
Whitehead Institute for Biomedical Research
Associate Professor
Massachusetts Institute of Technology

Dr. Nancy Leveson
Professor
Information and Computer Science Department
University of California at Irvine

Dr. Elliott Levinthal
Professor - Emeritus
Department of Mechanical Engineering
Stanford University

Dr. Alfred K. Mann
Professor of Physics, Emeritus
University of Pennsylvania

Dr. John C. Mather
COBE Project Scientist
National Aeronautics and Space Administration

Mr. Douglas McCormick
Editorial Director and Editor
Nature Publishing Co. & Bio/Technology Magazine

Dr. Melanie Mitchell
Assistant Professor
Santa Fe Institute

Dr. Marvin Moss
Deputy Director
Scripps Institute for Oceanography

Dr. Arthur R. M. Nowell
Professor and Director
School of Oceanography
University of Washington

1992 Participant List, cont.

Dr. Gilbert S. Omenn
Dean, School of Public Health/Community Medicine
University of Washington

Dr. Diane B. Paul
Professor of Political Science
University of Massachusetts - Boston

Dr. William D. Phillips
Physicist
National Institute of Standards and Technology

Dr. Rudolf A. Raff
Director
Institute for Molecular and Cellular Biology
Professor of Biology
Indiana University

Dr. Norman F. Ramsey
Higgins Professor of Physics, Emeritus
Harvard University

Dr. Maureen E. Raymo
Assistant Professor
Department of Geology and Geophysics
University of California at Berkeley

Dr. Vera C. Rubin
Staff Member
Department of Terrestrial Magnetism
Carnegie Institution of Washington

Dr. Jonas E. Salk
Founding Director
Distinguished Professor of International Health Sciences
Salk Institute for Biological Studies

Dr. David N. Schramm
Louis Block Professor in the Physical Sciences
University of Chicago

1992 Participant List, cont.

Ms. Barbara Schulz
High School Science Teacher
Shorewood High School

Dr. Stephen Sackett
Staff Astronomer
Observatories of the Carnegie Institution of Washington

Dr. L. Michael Simmons, Jr.
Vice President, Academic Affairs
Santa Fe Institute

Mr. William (Skip) A. Stiles
Legislative Director
Committee on Science, Space, and Technology
U.S. House of Representatives

Dr. A. Douglas Stone
Professor of Applied Physics and Physics
Yale University

Dr. Jack W. Szostak
Professor of Genetics
Harvard Medical School/Massachusetts General Hospital

Dr. Albert H. Teich
Director, Science and Public Policy Programs
American Association for the Advancement of Science

Mr. Michael A. Teitlebaum
Program Officer
Alfred P. Sloan Foundation

Dr. Michael Telson
Senior Analyst
Committee on the Budget
U.S. House of Representatives

Dr. J. Anthony Tyson
DMTS
American Telephone & Telegraph

1992 Participant List, cont.

Dr. Irving L. Weissman
Professor of Pathology
Stanford University School of Medicine

Dr. Clifford M. Will
Professor and Chairman
Department of Physics
Washington University

APPENDIX C:

1992 COLLOQUIUM STEERING COMMITTEE MEMBERS

**1992 KEYSTONE SCIENTIST TO SCIENTIST COLLOQUIUM
PROJECT STEERING COMMITTEE**

Chairman:

Dr. Eric S. Lander
Member
The Whitehead Institute for Biomedical Research

Co-Chairman:

Dr. Ronald E. Cape
Chairman
Darwin Technologies, Inc.

Members:

Dr. Eric G. Adelberger
Professor of Physics
University of Washington

Dr. Berni J. Alder
Group Leader
Lawrence Livermore Laboratories

Dr. Mary Clutter
Assistant Director
National Science Foundation

Mr. Robert W. Craig
President
The Keystone Center

Dr. Edward A. Feigenbaum
Professor of Computer Science
Stanford University

Dr. Margaret J. Geller
Professor of Astronomy
Harvard/Smithsonian Center for Astrophysics

Dr. David Gross
Professor of Physics
Princeton University

Dr. Leroy Hood
William Gates III Prof. of Molecular Biotechnology
University of Washington

Dr. Daniel J. Kevles
Koepfli Professor of the Humanities
California Institute of Technology

Dr. Gilbert S. Omenn
Dean, School of Public Health/Community Medicine
University of Washington

APPENDIX D:

**EDITORIAL ON THE 1992 SCIENTIST TO SCIENTIST COLLOQUIUM FROM
THE OCTOBER 1992 ISSUE OF BIO/TECHNOLOGY MAGAZINE**

FIRST WORD/

LIGHT AND VERITY

By Douglas McCormick

There was a hint of the biblical—light and the beginnings of things—about the Keystone Center's Scientist to Scientist meeting, an August gathering of some seventy august American scientists.

Ron Cape (ex-Cetus, ex-Chiron, and now starting a new company called Darwin Molecular Technologies) and the non-profit Keystone Center started the conference a year ago to do something that other august groups—from the National Academy to the faculties of big research universities—do not: bring together first-rate scientists from many disciplines to learn what is happening on the frontiers of fields far removed from their own.

Written words—and only a few hundred of them, at that—can scarcely convey the resulting excitement. Remember when the doors of science first opened for you, when you first peered inside and saw the...well, grandeur? Remember when the new concepts and new insights seeped into your very dreams and transformed the way you looked at the waking world?

At its best, that's what Keystone was like—six different versions of the very best introductory science course you ever had (David Baltimore, Irving Weissman, and Leroy Hood taught introductory immunology), delivered to a roomful of students mostly unfamiliar with the material, but eager, intelligent, critical (in the most constructive sense), and questioning.

LET THERE BE LIGHT

And so it went for six days, often from eight in the morning to after ten at night.

Cosmologists peered back in time toward the great wall, tracking photons almost to the instant they first condensed out of the blazing primordial cloud to produce the very lumpy universe we now see around us.

Biophysicists traced the picosecond pulses of chlorophyll's astounding network of molecular antennae, as they trap light and funnel its fire into the maw of the chloroplast's reaction center for conversion into living energy.

Quantum physicists brought time almost to a standstill, making "optical molasses"—and the world's most precise clocks— from finely tuned laser light, a honey trap that slows atoms to crawl, cooling them to within a few thousandths of a degree of absolute zero.

Evolutionary biologists squinted back some three billion years to the beginnings of life on earth—perhaps as fortuitous tangles of self-replicating RNA captured, two by two, in natural liposome, combining and redividing in some gently lapping Precambrian surf.

Computer scientists, too, acknowledged the power of the "evolutionary method," as they described arthropoid robots that walk and stalk, and computer programs that manage their own evolution to produce rock videos and super-efficient sorting algorithms.

QUESTIONS

It was a time for asking the stupid questions and musing on the big ones. A geophysicist could ask, relatively unself-consciously, "What is a cell?" A Nobel laureate physician could ask, "What is time?"

A prominent biologist could aver, "Evolution stopped when humanity invented medicine, but before too long, we will be altering ourselves intentionally. It will happen."

"Or perhaps," an artificial-intelligence guru could retort, "this will be the age in which the evolution of electronic life succeeds the evolution of chemical life."

Perhaps.

Amidst this meeting's melding of Darwinian method and the majesty of creation, though, ran the subtext of a verse from Genesis:

Now the whole earth had one language and few words. And as men migrated... they said to one another... "Come, let us build ourselves a city, and a tower with its top in the heavens, and let us make a name for ourselves, lest we be scattered abroad upon the face of the whole earth."

And the Lord came down to see the city and the tower, which the sons of men had built. And the Lord said, "Behold, they are one people, and they have all one language; and this is only the beginning of what they will do; and nothing that they propose to do will now be impossible for them. Come, let us go down, and there confuse their language, that they may not understand one another's speech." So the Lord scattered them abroad from there over the face of all the earth, and they left off building the city.

For a long time, it seemed that the edifice of Western science—humanity's most profound and beautiful artistic achievement, whatever else it may be—was doomed to become a self-limiting Babel of isolated disciplines scattered abroad over the face of the earth, each cut off from the others by its own parochial obsessions and impenetrable jargon. Impious as it may be, we still yearn to build those towers with their tops in heaven, spires not of stone and mortar but of understanding. And the purpose of meetings like Keystone's is to teach us each the other's tongue, so that all can share in the execution and the plan.

The point of all this is synthesis and synergy—the very recipe that created and sustains biotechnology, among other things. We have said before that biotechnology is about the crossing of boundaries—disciplinary, national, species, it doesn't matter. Well, it seems that this may have been too narrow a view. After a week of talking with computer scientists taking lessons from biology, and biologists learning from the physicists how to look even more closely at fundamental life processes, and on and on in a web of new insights and ideas... For a moment, it seemed that all boundaries were in jeopardy—that truly nothing they proposed to do would be impossible to them.

Final Technical Report
August, 1992

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